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DATE: Sunday, September 19, 2004

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| <input type="checkbox"/> | L4 | 2001 | 18 |
| <input type="checkbox"/> | L3 | L1 same (ligand or bind or binding) | 68 |
| <input type="checkbox"/> | L2 | L1 same (ligand or bind\$) | 68 |
| <input type="checkbox"/> | L1 | ftsz same (alloster\$ or activat\$ or inhibit\$) | 95 |

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FILE 'MEDLINE' ENTERED AT 10:26:46 ON 19 SEP 2004

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=> s ftsz and (alloster? or activat? or inhibit?)
L1 382 FTSZ AND (ALLOSTER? OR ACTIVAT? OR INHIBIT?)

=> s l1 and (ligand or bind?)
L2 126 L1 AND (LIGAND OR BIND?)

=> s l2 and py<2001
L3 73 L2 AND PY<2001

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L4 ANSWER 1 OF 47 MEDLINE on STN
AN 2001010736 MEDLINE
DN PubMed ID: 10970844
TI CtrA mediates a DNA replication checkpoint that prevents cell division in
Caulobacter crescentus.
AU Wortinger M; Sackett M J; Brun Y V
CS Department of Biology and Department of Chemistry, Indiana University,
Bloomington, IN 47405, USA.
NC GM07757 (NIGMS)
GM51986 (NIGMS)
SO EMBO journal, *** (2000 Sep 1)*** 19 (17) 4503-12.
Journal code: 8208664. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200010
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001024
AB Coordination of DNA replication and cell division is essential in order to
ensure that progeny cells inherit a full copy of the genome. Caulobacter
crescentus divides asymmetrically to produce a non-replicating swarmer
cell and a replicating stalked cell. The global response regulator CtrA
coordinates DNA replication and cell division by repressing replication
initiation and transcription of the early cell division gene ***ftsZ***
in swarmer cells. We show that CtrA also mediates a DNA replication
checkpoint of cell division by regulating the late cell division genes
ftsQ and ftsA. CtrA ***activates*** transcription of the P(QA)
promoter that co-transcribes ftsQA, thus regulating the ordered expression
of early and late cell division proteins. Cells ***inhibited*** for
DNA replication are unable to complete cell division. We show that CtrA
is not synthesized in pre-divisional cells in which replication has been
inhibited, preventing the transcription of P(QA) and cell
division. Replication ***inhibition*** prevents the
activation of the ctrA P2 promoter, which normally depends on CtrA
phosphorylation. This suggests the possibility that CtrA phosphorylation
may be affected by replication ***inhibition***.

L4 ANSWER 2 OF 47 MEDLINE on STN
AN 2000327576 MEDLINE
DN PubMed ID: 10869074
TI Analysis of MinC reveals two independent domains involved in interaction
with MinD and ***FtsZ***.
AU Hu Z; Lutkenhaus J
CS Department of Microbiology, Molecular Genetics and Immunology, University
of Kansas Medical Center, Kansas City 66160, USA.
NC GM29764 (NIGMS)
SO Journal of bacteriology, *** (2000 Jul)*** 182 (14) 3965-71.
Journal code: 2985120R. ISSN: 0021-9193.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 20000811
Last Updated on STN: 20030111
Entered Medline: 20000802

AB In *Escherichia coli* ***FtsZ*** assembles into a Z ring at midcell while assembly at polar sites is prevented by the min system. MinC, a component of this system, is an ***inhibitor*** of ***FtsZ*** assembly that is positioned within the cell by interaction with MinDE. In this study we found that MinC consists of two functional domains connected by a short linker. When fused to MalE the N-terminal domain is able to ***inhibit*** cell division and prevent ***FtsZ*** assembly in vitro. The C-terminal domain interacts with MinD, and expression in wild-type cells as a MalE fusion disrupts min function, resulting in a minicell phenotype. We also find that MinC is an oligomer, probably a dimer. Although the C-terminal domain is clearly sufficient for oligomerization, the N-terminal domain also promotes oligomerization. These results demonstrate that MinC consists of two independently functioning domains: an N-terminal domain capable of ***inhibiting*** ***FtsZ*** assembly and a C-terminal domain responsible for localization of MinC through interaction with MinD. The fusion of these two independent domains is required to achieve topological regulation of Z ring assembly.

L4 ANSWER 3 OF 47 MEDLINE on STN DUPLICATE 1
AN 2000177835 MEDLINE
DN PubMed ID: 10712701
TI Non-hydrolysable GTP-gamma-S stabilizes the ***FtsZ*** polymer in a GDP-bound state.

AU Scheffers D J; den Blaauwen T; Driessen A J
CS Department of Microbiology, Groningen Biomolecular Sciences and Biotechnology Institute, University of Groningen, Kerklaan 30, 9751 NN Haren, The Netherlands.

SO Molecular microbiology, *** (2000 Mar) *** 35 (5) 1211-9.
Journal code: 8712028. ISSN: 0950-382X.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200004

ED Entered STN: 20000421

Last Updated on STN: 20000421

Entered Medline: 20000413

AB ***FtsZ***, a tubulin homologue, forms a cytokinetic ring at the site of cell division in prokaryotes. The ring is thought to consist of polymers that assemble in a strictly GTP-dependent way. GTP, but not guanosine-5'-O-(3-thiotriphosphate) (GTP-gamma-S), has been shown to induce polymerization of ***FtsZ***, whereas in vitro Ca²⁺ is known to ***inhibit*** the GTP hydrolysis activity of ***FtsZ***. We have studied ***FtsZ*** dynamics at limiting GTP concentrations in the presence of 10 mM Ca²⁺. GTP and its non-hydrolysable analogue GTP-gamma-S ***bind*** ***FtsZ*** with similar affinity, whereas the non-hydrolysable analogue guanylyl-imidodiphosphate (GMP-PNP) is a poor substrate. Preformed ***FtsZ*** polymers can be stabilized by GTP-gamma-S and are destabilized by GDP. As more than 95% of the nucleotide associated with the ***FtsZ*** polymer is in the GDP form, it is concluded that GTP hydrolysis by itself does not trigger ***FtsZ*** polymer disassembly. Strikingly, GTP-gamma-S exchanges only a small portion of the ***FtsZ*** polymer-bound GDP. These data suggest that ***FtsZ*** polymers are stabilized by a small fraction of GTP-containing ***FtsZ*** subunits. These subunits may be located either throughout the polymer or at the polymer ends, forming a GTP cap similar to tubulin.

L4 ANSWER 4 OF 47 MEDLINE on STN DUPLICATE 2
AN 2000145423 MEDLINE
DN PubMed ID: 10679194
TI Isolation and characterization of dcw cluster from *Streptomyces collinus* producing kirromycin.

AU Mikulik K; Zhulanova E; Kratky M; Kofronova O; Benada O
CS Institute of Microbiology, Academy of Sciences of the Czech Republic,

Videnska 1083, Prague 4, 142 20, Czech Republic.

SO Biochemical and biophysical research communications, *** (2000 Feb 16) ***

268 (2) 282-8.
 Journal code: 0372516. ISSN: 0006-291X.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200003
 ED Entered STN: 20000327
 Last Updated on STN: 20000327
 Entered Medline: 20000310

AB A 4.5-kb BamHI fragment of chromosomal DNA of *Streptomyces collinus* containing gene *****ftsZ***** was cloned and sequenced. Upstream of *****ftsZ***** are localized genes *ftsQ*, *murG*, and *ftsW*, and downstream is *yfiH*. Gene *ftsA* is not adjacent to *****ftsZ***** or other genes of the cloned fragment. Protein *****FtsZ***** was isolated and characterized with respect to its *****binding***** to GTP and GTPase activity. The *****binding***** of GTP to *****FtsZ***** was Ca(2+) or Mg(2+) dependent with an optimum at 10 mM. The rate of GTP hydrolysis by *****FtsZ***** was stimulated by KCl. The presence of Ca(2+) (3-5 mM) resulted in a significant increase of GTPase activity. Higher concentrations of Ca(2+) than 5 mM had an *****inhibitory***** effect on GTPase activity. These results indicate that divalent ions (Ca(2+) or Mg(2+)) can be involved in regulation of GTP *****binding***** and hydrolysis of *****FtsZ*****. The maximum level of *****FtsZ***** was detected in aerial mycelium when spiral loops and sporulation septa were formed. *****FtsZ***** is degraded after finishing sporulation septa.
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L4 ANSWER 5 OF 47 MEDLINE on STN
 AN 2000403902 MEDLINE
 DN PubMed ID: 10908725
 TI The HslU ATPase acts as a molecular chaperone in prevention of aggregation of Sula, an *****inhibitor***** of cell division in *Escherichia coli*.
 AU Seong I S; Oh J Y; Lee J W; Tanaka K; Chung C H
 CS School of Biological Sciences, College of Natural Sciences, Seoul National University, Seoul 151-742, South Korea.
 SO FEBS letters, *******(2000 Jul 21)******* 477 (3) 224-9.
 Journal code: 0155157. ISSN: 0014-5793.
 CY Netherlands
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200008
 ED Entered STN: 20000901
 Last Updated on STN: 20021217
 Entered Medline: 20000818

AB HslVU is an ATP-dependent protease consisting of two multimeric components: the HslU ATPase and the HslV peptidase. Sula, which is an *****inhibitor***** of cell division and has high tendency of aggregation, is degraded by HslVU protease. Here we show that HslU plays a role not only as a regulatory component for the HslV-mediated proteolysis but also as a molecular chaperone. Purified HslU prevented aggregation of Sula in a concentration-dependent fashion. This chaperone activity required oligomerization of HslU subunits, which could be achieved by ATP-*****binding***** or in the presence of high HslU protein concentrations. *hsl* mutation reduced the Sula-mediated *****inhibition***** of cell growth and this effect could be reversed upon overproduction of HslU, suggesting that HslU promotes the ability of Sula to block cell growth through its chaperone function. Thus, HslU appears to have two antagonistic functions: one as a chaperone for promotion of the ability of Sula in cell growth *****inhibition***** by preventing Sula aggregation and the other as the regulatory component for elimination of Sula by supporting the HslV-mediated degradation.

L4 ANSWER 6 OF 47 MEDLINE on STN
 AN 2000025414 MEDLINE
 DN PubMed ID: 10555966
 TI Self- *****activation***** of guanosine triphosphatase activity by oligomerization of the bacterial cell division protein *****FtsZ*****.
 AU Sossong T M Jr; Brigham-Burke M R; Hensley P; Pearce K H Jr
 CS Department of Anti-Infectives Research, SmithKline Beecham Pharmaceuticals, 1250 South Collegeville Road, Collegeville, Pennsylvania 19426, USA.. Thomas_M_Sossong@sbphrd.com
 SO Biochemistry, *******(1999 Nov 9)******* 38 (45) 14843-50.
 Journal code: 0370623. ISSN: 0006-2960.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199912
ED Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991220

AB The essential bacterial cell division protein *****FtsZ***** (filamentation temperature-sensitive protein Z) is a distant homologue to the eukaryotic cytoskeletal protein tubulin. We have examined the GTP hydrolytic activity of *Escherichia coli* *****FtsZ***** using a real-time fluorescence assay that monitors phosphate production. The GTPase activity shows a dramatic, nonlinear dependence on *****FtsZ***** concentration, with activity only observed at enzyme concentrations greater than 1 μM . At 5 μM *****FtsZ*****, we have determined a K_m of 82 μM GTP and a V_{max} of 490 $\text{nmol of P(i) min}^{-1}$ (mg of protein) $^{-1}$. Hydrolysis of GTP requires Mg^{2+} and other divalent cations substitute only poorly for this requirement. We have compared the concentration dependence of *****FtsZ***** GTPase activity with the oligomeric state by use of analytical ultracentrifugation and chemical cross-linking. Equilibrium analytical ultracentrifugation experiments show that *****FtsZ***** exists as 68% dimer and 13% trimer at 2 μM total protein concentration. Chemical cross-linking of *****FtsZ***** also shows that monomer, dimer, trimer, and tetramer species are present at higher ($>2 \mu\text{M}$) *****FtsZ***** concentrations. However, as shown by analytical centrifugation, GDP-bound *****FtsZ***** is significantly shifted to the monomeric state, which suggests that GTP hydrolysis regulates polymer destabilization. We also monitored the effect of nucleotide and metal ion on the secondary structure of *****FtsZ*****; nucleotide yielded no evidence of structural changes in *****FtsZ*****, but both Mg^{2+} and Ca^{2+} had significant effects on secondary structure. Taken together, our results support the hypothesis that Mg^{2+} -dependent GTP hydrolysis by *****FtsZ***** requires oligomerization of *****FtsZ*****. On the basis of these results and structural comparisons with the α - β tubulin dimer, GTP is likely hydrolyzed in a shared active site formed between two monomer subunits.

L4 ANSWER 7 OF 47 MEDLINE on STN
AN 2000079565 MEDLINE
DN PubMed ID: 10611296

TI The MinC component of the division site selection system in *Escherichia coli* interacts with *****FtsZ***** to prevent polymerization.
AU Hu Z; Mukherjee A; Pichoff S; Lutkenhaus J
CS Department of Microbiology, University of Kansas Medical Center, Kansas City, KS 66160, USA.
NC GM 29764 (NIGMS)
SO Proceedings of the National Academy of Sciences of the United States of America, *******(1999 Dec 21)******* 96 (26) 14819-24.
Journal code: 7505876. ISSN: 0027-8424.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200001
ED Entered STN: 20000204
Last Updated on STN: 20030111
Entered Medline: 20000127

AB Positioning of the Z ring at the midcell site in *Escherichia coli* is assured by the min system, which masks polar sites through topological regulation of MinC, an *****inhibitor***** of division. To study how MinC *****inhibits***** division, we have generated a MalE-MinC fusion that retains full biological activity. We find that MalE-MinC interacts with *****FtsZ***** and prevents polymerization without *****inhibiting***** *****FtsZ*****'s GTPase activity. MalE-MinC19 has reduced ability to *****inhibit***** division, reduced affinity for *****FtsZ*****, and reduced ability to *****inhibit***** *****FtsZ***** polymerization. These results, along with MinC localization, suggest that MinC rapidly oscillates between the poles of the cell to destabilize *****FtsZ***** filaments that have formed before they mature into polar Z rings.

L4 ANSWER 8 OF 47 MEDLINE on STN
AN 1999296575 MEDLINE
DN PubMed ID: 10368140
TI The ATP-dependent HslVU/ClpQY protease participates in turnover of cell

DUPLICATE 3

division ***inhibitor*** Sula in Escherichia coli.
 AU Kanemori M; Yanagi H; Yura T
 CS HSP Research Institute, Kyoto Research Park, Kyoto 600-8813, Japan.
 SO Journal of bacteriology, *** (1999 Jun)*** 181 (12) 3674-80.
 Journal code: 2985120R. ISSN: 0021-9193.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199907
 ED Entered STN: 19990727
 Last Updated on STN: 20021008
 Entered Medline: 19990715
 AB Escherichia coli mutants lacking activities of all known cytosolic ATP-dependent proteases (Lon, ClpAP, ClpXP, and HslVU), due to double deletions [Delta hslVU and Delta (clpPX-lon)], cannot grow at low (30 degrees C) or very high (45 degrees C) temperatures, unlike those carrying either of the deletions. Such growth defects were particularly marked when the deletions were introduced into strain MG1655 or W3110. To examine the functions of HslVU and other proteases further, revertants that can grow at 30 degrees C were isolated from the multiple-protease mutant and characterized. The revertants were found to carry a suppressor affecting either ***ftsZ*** (encoding a key cell division protein) or sula (encoding the Sula ***inhibitor***, which ***binds*** and ***inhibits*** ***FtsZ***). Whereas the ***ftsZ*** mutations were identical to a mutation known to produce a protein refractory to Sula ***inhibition***, the sula mutations affected the promoter-operator region, reducing synthesis of Sula. These results suggested that the growth defect of the parental double-deletion mutant at a low temperature was due to the accumulation of excess Sula without DNA-damaging treatment. Consistent with these results, Sula in the double-deletion mutant was much more stable than that in the Delta (clpPX-lon) mutant, suggesting that Sula can be degraded by HslVU. As expected, purified HslVU protease degraded Sula (fused to the maltose- ***binding*** protein) efficiently in an ATP-dependent manner. These results suggest that HslVU as well as Lon participates in the in vivo turnover of Sula and that HslVU becomes essential for growth when the Lon (and Clp) protease level is reduced below a critical threshold.

L4 ANSWER 9 OF 47 MEDLINE on STN
 AN 1999406903 MEDLINE
 DN PubMed ID: 10476030
 TI Delayed nucleoid segregation in Escherichia coli.
 AU Huls P G; Vischer N O; Woldringh C L
 CS Institute for Molecular Cell Biology, BioCentrum Amsterdam, University of Amsterdam, Kruislaan 316, 1098 SM Amsterdam, The Netherlands.
 SO Molecular microbiology, *** (1999 Sep)*** 33 (5) 959-70.
 Journal code: 8712028. ISSN: 0950-382X.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199910
 ED Entered STN: 19991101
 Last Updated on STN: 19991101
 Entered Medline: 19991021
 AB To study the role of cell division in the process of nucleoid segregation, we measured the DNA content of individual nucleoids in isogenic Escherichia coli cell division mutants by image cytometry. In pbpB(Ts) and ***ftsZ*** strains growing as filaments at 42 degrees C, nucleoids contained, on average, more than two chromosome equivalents compared with 1.6 in wild-type cells. Because similar results were obtained with a pbpB recA strain, the increased DNA content cannot be ascribed to the occurrence of chromosome dimers. From the determination of the amount of DNA per cell and per individual nucleoid after rifampicin ***inhibition***, we estimated the C and D periods (duration of a round of replication and time between termination and cell division respectively), as well as the D' period (time between termination and nucleoid separation). Compared with the parent strain and in contrast to ftsQ, ftsA and ***ftsZ*** mutants, pbpB(Ts) cells growing at the permissive temperature (28 degrees C) showed a long D' period (42 min versus 18 min in the parent) indicative of an extended segregation time. The results indicate that a defective cell division protein such as PbpB not only affects the division process but also plays a role in the last stage of DNA segregation. We propose that PbpB is involved in the

assembly of the divisome and that this structure enhances nucleoid segregation.

L4 ANSWER 10 OF 47 MEDLINE on STN DUPLICATE 4
AN 2000042187 MEDLINE
DN PubMed ID: 10572304
TI An assessment of the role of intracellular free Ca²⁺ in E. coli.
AU Holland I B; Jones H E; Campbell A K; Jacq A
CS Institut de Genetique et Microbiologie, UMR CNRS 8621, Universite
Paris-Sud, Batiment 409,0, 91405 Orsay Cedex, France.
SO Biochimie, *** (1999 Aug-Sep) *** 81 (8-9) 901-7. Ref: 44
CY Journal code: 1264604. ISSN: 0300-9084.
DT France
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200001
ED Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000106
AB We have previously proposed that fluctuations in Ca(2+) levels should play an important role in bacteria as in eukaryotes in regulating cell cycle events (Norris et al., J. Theor. Biol. 134 (1998) 341-350). This proposal implied the presence of Ca(2+) uptake systems in bacteria, cell cycle mutants simultaneously defective in Ca(2+)-homeostasis, and perturbation of cell cycle processes when cellular Ca(2+) levels are depleted. We review the properties of new cell cycle mutants in E. coli and B. subtilis resistant to ***inhibitors*** of calmodulin, PKC or Ca(2+)-channels; the evidence for Ca(2+)- ***binding*** proteins including Acp and ***FtsZ*** ; and Ca(2+)-transporters. In addition, the effects of EGTA and verapamil (a Ca(2+) channel ***inhibitor***) on growth, protein synthesis and cell cycle events in E. coli are described. We also describe new measurements of free Ca(2+)-levels, using aequorin, in E. coli. Several new cell cycle mutants were obtained using this approach, affecting either initiation of DNA replication or in particular cell division at non-permissive temperature. Several of the mutants were also hypersensitive to EGTA and or Ca(2+). However, none of the mutants apparently involved direct alteration of a drug target and surprisingly in some cases involved specific tRNAs or a tRNA synthetase. The results also indicate that the expression of several genes in E. coli may be regulated by Ca(2+). Cell division in particular appears very sensitive to the level of cell Ca(2+), with the frequency of division clearly reduced by EGTA and by verapamil. However, whilst the effect of EGTA was clearly correlated with depletion of cellular Ca(2+) including free Ca(2+), this was not the case with verapamil which appears to change membrane fluidity and the consequent activity of membrane proteins. Measurement of free Ca(2+) in living cells indicated levels of 200-300 nM, tightly regulated in wild type cells in exponential phase, somewhat less so in stationary phase, with apparently La(2+)-sensitive PHB-polyphosphate complexes involved in Ca(2+) influx. The evidence reviewed increasingly supports a role for Ca(2+) in cellular processes in bacteria, however, any direct link to the control of cell cycle events remains to be established.

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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

FULL ESTIMATED COST

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SESSION

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12.63

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